

May 14, 1945

Dr. Van H. Potter
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University of Wisconsin
Madison, Wisconsin

Dear Dr. Potter;

I greatly appreciate your kind letter of May 9th and the possibility you suggested in it. Let me say immediately that I am definitely interested and am looking forward to the opportunity of discussing it at greater length. The activity and stimulation of your group are well enough known that I feel certain I would have much to gain from contact with it.

You requested some idea of my background. I may briefly summarize it as follows: I received my B.S. from the College of the City of New York in 1940 after being interrupted by a fellowship in physiology which was supposed to have lasted for 6 months but actually stretched out to $2\frac{1}{2}$ years. Since I was getting quite a bit of biology in my extra-curricular work I decided to devote my more formal training to the other sciences. I therefore majored in physics and minored in mathematics and chemistry as an undergraduate. In 1941, while working on a Rockefeller Foundation grant, I started graduate work in general physiology at Columbia University under Dr. H. Burr Steinbach. When he left in 1942 for Washington U. he took me along with him and I completed my doctorates at the end of 1943, having majored in physiology and minored in mathematics and biochemistry. My thesis was on enzymatic adaptation. While completing my doctorates I held lectureships in Physics, Applied Mathematics and General Physiology. When the demand for mathematics and physics instruction subsided somewhat I accepted an appointment in the Department of Bacteriology at the Medical School.

Fundamentally I am a general cellular physiologist. To give you some idea of the kind of work I have done I have enclosed a complete list of publications and am sending under separate cover those of the available reprints which you do not have. You may perhaps find the 1937 paper published in the Jour. of Genetics of some interest (see particularly the discussion). This work represents the beginning of my interest in problems of cellular variation and differentiation and I was convinced then that microorganisms held the key to solution of many of the puzzles. We amassed a lot of data on the question but this was the only paper we published for several reasons. For one thing the details were always obscured by the uncontrollable genetics of bacteria. Perhaps more important, we got very little encouragement at that time and could convince no one that a study of microorganismic populations could contribute to an understanding of tissue variation and differentiation. It wasn't until almost 7 years later that I could return to the problem with a more suitable material (yeast) and environment.

With reference to the discussion you enclosed, I am in fundamental agreement with it although on several points there may be room for further discussion which I hope we will be able to indulge in when I get up your way. For the moment I should briefly like to note the following. You state; "Evidently one could not prove the presence of a gene for an

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enzyme whose action was inseparably connected with the maintenance of life .." This is certainly correct if one considers segregation data as the only valid proof for the existence of genes. However a careful analysis of survival curves during exposure to various lethal agents (e.g. radiation, heat, poisons, etc.) indicate the existence of 'inheritable units' whose inactivation leads to death. One might conceivably accept such data as strong indications for the existence of genes whose absence is lethal. There are other aspects of this problem I hope to discuss with you but in any case a qualification of the above statement might be safer although it may be admitted that 'safety' per se is a pretty monotonous thing to strive for.

With reference to Karstrom, I may be wrong, but it is my impression that he was not thinking of 'vitally essential' enzymes when he set up his definition of the constitutive enzyme. It seems to me that he was focussing his attention on the environment and was I believe, seeking to emphasize differences in response to presence and absence of substrate. He thus ended up with a qualitative scheme of classification of enzymes altho it seems probable that the difference is fundamentally quantitative in nature. Please bear in mind that I am biased on this subject as you probably already have noted.

Thanks again for your letter and heres hoping we can get together soon.

Sincerely yours,

S. Spiegelman

SS/McK